

1. (Amended) A targeting molecule linked to at least one biological agent, wherein said targeting molecule comprises a polypeptide that [:
(a) forms a closed covalent loop; and
(b) contains at least three peptide domains having β -sheet character, each of the domains being separated by domains lacking β -sheet character;] comprises a J chain or a portion thereof that specifically binds to an epithelial basolateral factor, wherein said polypeptide is not full length dimeric IgA;

and wherein said targeting molecule is further linked to a peptide sequence that directs delivery of the biological agent to a carcinoma cell, a nucleus or an endoplasmic reticulum.

2. (Amended) A targeting molecule linked to at least one biological agent according to claim 1 wherein said targeting molecule is covalently linked to at least one biological agent.

3. (Amended) A targeting molecule linked to at least one biological agent according to claim 2 wherein said molecule contains at least one cysteine residue linked to the biological agent(s).

4. (Amended) A targeting molecule linked to at least one biological agent according to claim 2 wherein said molecule is linked to a biological agent via a peptide bond.

5. (Amended) A targeting molecule linked to at least one biological agent according to claim 1 wherein said molecule is noncovalently linked to at least one biological agent.

6. (Amended) A targeting molecule linked to at least one biological agent according to claim 1 wherein said polypeptide comprises [amino acid residues 13-71 and 93-101 of SEQ ID NO:1,] Cys Lys Cys Ala Arg Ile Thr Ser Arg Ile Ile Arg Ser Ser Glu Asp Pro Asn Glu Asp Ile Val Glu Arg Asn Ile Arg Ile Ile Val Pro Leu Asn Asn Arg Glu Asn Ile Ser Asp Pro Thr Ser Pro Leu Arg Thr Arg Pro Val Tyr His Leu Ser Asp Leu Cys Lys Lys Asp Glu Asp Ser Ala Thr Glu Thr Cys (SEQ ID NO:114), [amino acid residues 13-71 and 93-99 of SEQ ID NO:2,] Cys Lys Cys Ala Arg Asp Ser Asp Ala Glu Thr Cys (SEQ ID NO:115), [amino acid residues 12-70 and 92-101 of SEQ ID NO:3,] Cys Met Cys Thr Arg Val Thr Ser Arg Ile Ile Pro Ser Thr Glu Asp Pro Asn Glu Asp Ile Val Glu Arg Asn Ile Arg Ile Val Val Pro Leu Asn Asn Arg Glu Asn Ile Ser Asp Pro Thr Ser Pro Leu Arg Arg Asn Pro Val Tyr His Leu Ser Asp Val Cys Lys Lys Asn Glu Asp Asp Gly Val Pro Glu Thr Cys (SEQ ID NO:116), [amino acid residues 12-70 and 92-100 of SEQ ID NO:4,] Cys Gln Cys Val Arg Ile Thr Ser Arg Ile Ile Arg Asp Pro Asp Asn Pro Ser Glu Asp Ile Val Glu Arg Asn Ile Arg Ile Ile

Val Pro Leu Asn Thr Arg Glu Asn Ile Ser Asp Pro Thr Ser Pro Leu Arg Thr Glu Pro Lys Tyr Asn Leu Ala Asn Leu Cys Lys Lys Pro Asp Asp Asp Tyr Ser Glu Thr Cys (SEQ ID NO:117), [amino acid residues 11-69 and 89-96 of SEQ ID NO:5,] Cys Lys Cys Val Lys Ile Ser Ser Arg Phe Val Pro Ser Thr Glu Arg Pro Gly Glu Glu Ile Leu Glu Arg Asn Ile Gln Ile Thr Ile Pro Thr Ser Ser Arg Met Xaa Ile Ser Asp Pro Tyr Ser Pro Leu Arg Thr Gln Pro Val Tyr Asn Leu Trp Asp Ile Cys Gln Lys Xaa Ser Xaa Pro Asp Asp Glu Cys (SEQ ID NO:118), or [and/or amino acid residues 3-61 and 79-88 of SEQ ID NO:6] Cys Met Cys Thr Arg Val Thr Ala Arg Ile Arg Gly Thr Arg Glu Asp Pro Asn Glu Asp Ile Val Glu Arg Tyr Ile Arg Ile Asn Val Pro Leu Lys Asn Arg Gly Asn Ile Ser Asp Pro Thr Ser Pro Leu Arg Asn Gln Pro Val Tyr His Leu Ser Pro Ser Cys Lys Lys Tyr Pro Asp Gln Gly Val Pro Gln Ser Cys (SEQ ID NO:119)[, or a variant thereof that differs only in conservative substitutions and/or modifications].

7. (Amended) A targeting molecule linked to at least one biological agent according to claim 1 wherein said polypeptide comprises the amino acid sequence encoded by nucleotides 1-414 of [recited in] SEQ ID NO:7[, or a variant thereof that differs only in conservative substitutions and/or modifications].

B₁ 8. (Amended) A targeting molecule linked to at least one biological agent according to claim 1 wherein said polypeptide comprises the amino acid sequence encoded by nucleotides 1-213 of [recited in] SEQ ID NO:8[, or a variant thereof that differs only in conservative substitutions and/or modifications].

9. (Amended) A targeting molecule linked to at least one biological agent according to claim 1 wherein said polypeptide comprises the amino acid sequence encoded by nucleotides 1-282 of [recited in] SEQ ID NO:13[, or a variant thereof that differs only in conservative substitutions and/or modifications].

10. (Amended) A targeting molecule linked to at least one biological agent according to claim 1 wherein said polypeptide contains at least four peptide domains having β -sheet character, separated by domains lacking β -sheet character.

11. (Amended) A targeting molecule linked to at least one biological agent according to claim 7 wherein said variant comprises [amino acid residues 13-99 of SEQ ID NO:2,] Cys Lys Cys Ala Arg Ile Thr Ser Arg Ile Ile Pro Ser Ala Glu Asp Pro Ser Gln Asp Ile Val Glu Arg Asn Val Arg Ile Ile Val Pro Leu Asn Ser Arg Glu Asn Ile Ser Asp Pro Thr Ser Pro Met Arg Thr Lys Pro Val Tyr His Leu Ser Asp Leu Cys Lys Lys Cys Asp Thr Thr Glu Val Glu Leu Glu Asp Gln Val Val Thr Ala Ser Gln Ser Asn Ile Cys Asp Ser Asp Ala Glu Thr Cys (SEQ ID NO:120), [amino acid residues 12-101 of SEQ ID NO:3,] Cys Met Cys Thr Arg Val Thr Ser Arg Ile Ile Pro Ser Thr Glu Asp Pro Asn Glu Asp Ile Val Glu Arg Asn Ile Arg Ile Val Val Pro Leu Asn Asn Arg Glu Asn Ile Ser Asp Pro Thr Ser Pro Leu Arg Arg Asn

Pro Val Tyr His Leu Ser Asp Val Cys Lys Lys Cys Asp Pro Val Glu Val Glu Leu Glu Asp Gln
Val Val Thr Ala Thr Gln Ser Asn Ile Cys Asn Glu Asp Asp Gly Val Pro Glu Thr Cys (SEQ ID
NO:121), [amino acid residues 12-100 of SEQ ID NO:4,]Cys Gln Cys Val Arg Ile Thr Ser
Arg Ile Ile Arg Asp Pro Asp Asn Pro Ser Glu Asp Ile Val Glu Arg Asn Ile Arg Ile Ile Val Pro
Leu Asn Thr Arg Glu Asn Ile Ser Asp Pro Thr Ser Pro Leu Arg Thr Glu Pro Lys Tyr Asn Leu
Ala Asn Leu Cys Lys Lys Cys Asp Pro Thr Glu Ile Glu Leu Asp Asn Gln Val Phe Thr Ala Ser
Gln Ser Asn Ile Cys Pro Asp Asp Asp Tyr Ser Glu Thr Cys (SEQ ID NO:122), [amino acid
residues 11-95 of SEQ ID NO:5,]Cys Lys Cys Val Lys Ile Ser Ser Arg Phe Val Pro Ser Thr
Glu Arg Pro Gly Glu Glu Ile Leu Glu Arg Asn Ile Gln Ile Thr Ile Pro Thr Ser Ser Arg Met
Xaa Ile Ser Asp Pro Tyr Ser Pro Leu Arg Thr Gln Pro Val Tyr Asn Leu Trp Asp Ile Cys Gln
Lys Cys Asp Pro Val Gln Leu Glu Ile Gly Gly Ile Pro Val Leu Ala Ser Gln Pro Xaa Xaa Ser
Xaa Pro Asp Asp Glu (SEQ ID NO:123) or [and/or amino acid residues 3-88 of SEQ ID
NO:6,]Cys Thr Arg Val Thr Ala Arg Ile Arg Gly Thr Arg Glu Asp Pro Asn Glu Asp Ile Val
Glu Arg Tyr Ile Arg Ile Asn Val Pro Leu Lys Asn Arg Gly Asn Ile Ser Asp Pro Thr Ser Pro
Leu Arg Asn Gln Pro Val Tyr His Leu Ser Pro Ser Cys Lys Lys Cys Asp Pro Tyr Glu Asp Gly
Val Val Thr Ala Thr Glu Thr Asn Ile Cys Tyr Pro Asp Gln Gly Val Pro Gln Ser Cys (SEQ ID
NO:124)], or a variant thereof that differs only in conservative substitutions and/or
modifications].

B1 12. (Amended) A targeting molecule linked to at least one biological agent according to claim 1 wherein said polypeptide further comprises a linear N-terminal domain.

13. (Amended) A targeting molecule linked to at least one biological agent according to claim 12 wherein said N-terminal domain comprises [amino acid residues 1-12 of SEQ ID NO:1,] Gln Glu Asp Glu Arg Ile Val Leu Val Asp Asn Lys (SEQ ID NO:125), [amino acid residues 1-12 of SEQ ID NO:2,]Gln Asp Glu Asn Glu Arg Ile Val Val Asp Asn Lys (SEQ ID NO:126), [amino acid residues 1-11 of SEQ ID NO:3,]Asp Asp Glu Ala Thr Ile Leu Ala Asp Asn Lys (SEQ ID NO:127), [amino acid residues 1-11 of SEQ ID NO:4,]Asp Asp Glu Ala Thr Ile Leu Ala Asp Asn Lys (SEQ ID NO:128), [amino acid residues 1-10 of SEQ ID NO:5,]Glu Gln Glu Tyr Ile Leu Ala Asn Asn Lys (SEQ ID NO:129) or [and/or amino acid residues 1-2 of SEQ ID NO:6,]Asn Lys[, or a variant thereof that differs only in conservative substitutions and/or modifications].

14. (Amended) A targeting molecule linked to at least one biological agent according to claim 1 wherein said polypeptide further comprises a C-terminal domain.

15. (Amended) A targeting molecule linked to at least one biological agent according to claim 14 wherein said C-terminal domain comprises a linear peptide having β -sheet character.

16. (Amended) A targeting molecule linked to at least one biological agent according to claim 12 wherein said linear peptide comprises [amino acid residues 102-108 of SEQ ID NO:1,] Tyr Thr Tyr Asp Arg Asn Lys (SEQ ID NO:130), [amino acid residues 100-106 of SEQ ID NO:2,] Tyr Thr Tyr Asp Arg Asn Lys (SEQ ID NO:131), [amino acid residues 102-108 of SEQ ID NO:3,] Tyr Met Tyr Asp Arg Asn Lys (SEQ ID NO:132), [amino acid residues 101-107 of SEQ ID NO:4,] Tyr Thr Tyr Asp Arg Asn Lys (SEQ ID NO:133) or [and/or amino acid residues 89-99 of SEQ ID NO:6,] Arg Asp Tyr Cys Pro Glu Leu Asp Arg Asn Lys (SEQ ID NO:134)[, or a variant thereof that differs only in conservative substitutions and/or modifications].

17. (Amended) A targeting molecule linked to at least one biological agent according to claim 14 wherein said C-terminal domain comprises a covalently closed loop.

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18. (Amended) A targeting molecule linked to at least one biological agent according to claim 17 wherein the covalently closed loop within said C-terminal domain comprises [amino acid residues 109-137 of SEQ ID NO:1,] Cys Tyr Thr Ala Val Val Pro Leu Val Tyr Gly Gly Glu Thr Lys Met Val Glu Thr Ala Leu Thr Pro Asp Ala Cys Tyr Pro Asp (SEQ ID NO:135), [amino acid residues 107-135 of SEQ ID NO:2,] Cys Tyr Thr Asn Arg Val Lys Leu Ser Tyr Arg Gly Gln Thr Lys Met Val Glu Thr Ala Leu Thr Pro Asp Ser Cys Tyr Pro Asp (SEQ ID NO:136), [amino acid residues 109-137 of SEQ ID NO:3,] Cys Tyr Thr Thr Met Val Pro Leu Arg Tyr His Gly Glu Thr Lys Met Val Gln Ala Ala Leu Thr Pro Asp Ser Cys Tyr Pro Asp (SEQ ID NO:137), [amino acid residues 108-136 of SEQ ID NO:4,] Cys Tyr Thr Thr Leu Val Pro Ile Thr His Arg Gly Val Thr Arg Met Val Lys Ala Thr Leu Thr Pro Asp Ser Cys Tyr Pro Asp (SEQ ID NO:138), [amino acid residues 96-119 of SEQ ID NO:5,] Cys Tyr Thr Thr Glu Val Asn Phe Lys Lys Lys Val Pro Leu Thr Pro Asp Ser Cys Tyr Glu Tyr Ser Glu (SEQ ID NO:139) or [and/or amino acid residues 100-128 of SEQ ID NO:6,] Cys Tyr Thr Val Leu Val Pro Pro Gly Tyr Thr Gly Glu Thr Lys Met Val Gln Asn Ala Leu Thr Pro Asp Ala Cys Tyr Pro Asp (SEQ ID NO:140)[, or a variant thereof that differs only in conservative substitutions and/or modifications].

19. (Amended) A targeting molecule linked to at least one biological agent, wherein said targeting molecule is a polypeptide [comprising a sequence recited in any one] selected from the group consisting of SEQ ID NO:1 - SEQ ID NO:6;

and wherein said targeting molecule is further linked to a peptide sequence that directs delivery of the biological agent to a carcinoma cell, a nucleus or an endoplasmic reticulum.

20. (Amended) A targeting molecule linked to at least one biological agent, wherein said targeting molecule is a polypeptide [comprising a sequence] encoded by nucleotides 1-414 of [recited in] SEQ ID NO:7;

and wherein said targeting molecule is further linked to a peptide sequence that directs delivery of the biological agent to a carcinoma cell, a nucleus or an endoplasmic reticulum.

21. (Amended) A targeting molecule linked to at least one biological agent, wherein said targeting molecule is a polypeptide [comprising a sequence] encoded by nucleotides 1-213 of [recited in] SEQ ID NO:8;

and wherein said targeting molecule is further linked to a peptide sequence that directs delivery of the biological agent to a carcinoma cell, a nucleus or an endoplasmic reticulum.

22. (Amended) A targeting molecule linked to at least one biological agent, wherein said targeting molecule is a polypeptide [comprising a sequence] encoded by nucleotides 1-282 of [recited in] SEQ ID NO:13;

and wherein said targeting molecule is further linked to a peptide sequence that directs delivery of the biological agent to a carcinoma cell, a nucleus or an endoplasmic reticulum.

24. (Amended) A targeting molecule linked to at least one biological agent according to claim 23 wherein said targeting molecule contains at least one cysteine residue linked to the biological agent(s).

25. (Amended) A targeting molecule linked to at least one biological agent according to claim 23 wherein said molecule is linked to a biological agent via a peptide bond.

26. (Amended) A targeting molecule linked to at least one biological agent according to claim 23 wherein said molecule is linked to a biological agent via a glycoside bond.

27. (Amended) A targeting molecule linked to at least one biological agent according to claim 23 wherein said molecule is linked to a biological agent via a phosphodiester bond.

28. (Amended) A targeting molecule linked to at least one biological agent according to any one of claims 19-22 wherein said molecule is noncovalently linked to at least one biological agent.

B3 30. (Amended) A targeting molecule according to claim 1 [or claim 29] wherein said biological agent is selected from the group consisting of enzymes, antibodies, single chain antigen binding proteins, antigen combining sites, [binding agents, inhibitors,] nucleic acids, carbohydrates and lipids.

31. (Amended) A pharmaceutical composition comprising a targeting molecule linked to at least one biological agent according to claim 1 [or claim 29], in combination with a pharmaceutically acceptable carrier.

36. (Amended) A targeting molecule linked to at least one biological agent, wherein said targeting molecule comprises a polypeptide that[:

(a) forms a closed covalent loop; and

(b) contains at least three peptide domains having β -sheet character, each of the domains being separated by domains lacking β -sheet character;]

comprises a J chain or a portion thereof that specifically binds to an epithelial basolateral factor;

wherein said targeting molecule is linked to at least one biological agent by a substrate for an intracellular or extracellular enzyme associated with or secreted from an epithelial barrier;

and wherein said targeting molecule is further linked to a peptide sequence that directs delivery of the biological agent to a carcinoma cell, a nucleus or an endoplasmic reticulum.

B4 37. (Amended) A targeting molecule linked to at least one biological agent according to claim 36, wherein said enzyme is selected from the group consisting of proteases, glycosidases, phospholipases, esterases, hydrolases, and nucleases.

38. (Amended) A targeting molecule linked to at least one biological agent, wherein said targeting molecule comprises a polypeptide that[:

(a) forms a closed covalent loop; and

(b) contains at least three peptide domains having β -sheet character, each of the domains being separated by domains lacking β -sheet character;]

comprises a J chain or a portion thereof that specifically binds to an epithelial basolateral factor;

wherein said targeting molecule is linked to at least one biological agent through a side chain of amino acids in an antibody combining site;

and wherein said targeting molecule is further linked to a peptide sequence that directs delivery of the biological agent to a carcinoma cell, a nucleus or an endoplasmic reticulum.

39. (Amended) A targeting molecule linked to at least one biological agent, wherein said targeting molecule comprises a polypeptide that[:

- (a) forms a closed covalent loop; and
- (b) contains at least three peptide domains having β -sheet character, each of the domains being separated by domains lacking β -sheet character;]

comprises a J chain or a portion thereof that specifically binds to an epithelial basolateral factor;

wherein the biological agent is not naturally associated with the targeting molecule, and wherein the biological agent is not iodine;

and wherein said targeting molecule is further linked to a peptide sequence that directs delivery of the biological agent to a carcinoma cell, a nucleus or an endoplasmic reticulum.

40. (Amended) A targeting molecule linked to at least one biological agent according to claim 39, wherein said biological agent is selected from the group consisting of enzymes, [binding agents, inhibitors,] antibodies, single chain antigen binding proteins, antigen combining sites, nucleic acids, carbohydrates and lipids.

41. A targeting molecule linked to at least one biological agent according to claim 39, wherein said biological agent comprises an antigen combining site.

Please cancel claim 29 without prejudice.

REMARKS

Reconsideration of the present application in view of the above amendments and the following remarks is respectfully requested. Claims 1-31 and 36-41 were pending. Claim 29 has been canceled without prejudice. Claims 1-22, 24-28, 30, 31 and 36-41 have been amended to more specifically recite the subject matter that Applicants regard as the subject invention. In particular, claims 1, 36 and 38-39 have been amended to recite that the polypeptide comprises a J chain or a portion thereof. Support for this amendment may be found, for example, in the specification at page 8, lines 29-30 and page 9, lines 11-14. Claims 1, 19, 36 and 38-39 have been amended to recite that the targeting molecule is linked to a peptide sequence that directs delivery of the biological agent to a carcinoma cell, a nucleus or an endoplasmic reticulum. Support for this amendment may be found, for example, within the specification at page 14, lines 3-4; page 19, line 27 – page 20, line 2; page 20, lines 14-16; and page 70, line 14 – page 72, line 2. Claim 19 has been amended to clarify that the polypeptide